Figure 1

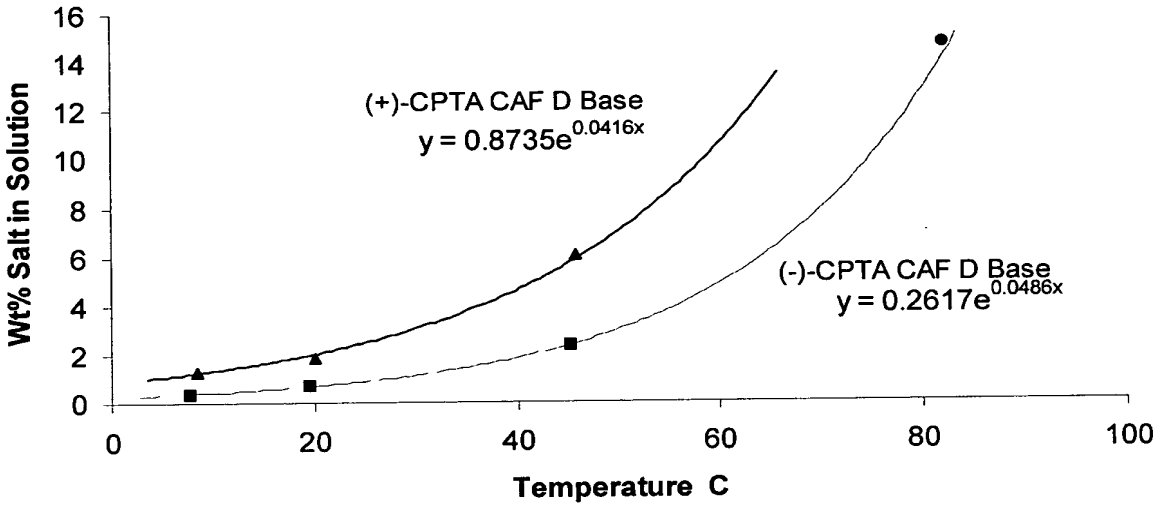
16
14
12
10
8
6
4
2
0
Wt% Salt in Solution
(+)-CPTA CAF D Base
y = 0.8735e^0.0416x
(-)-CPTA CAF D Base
y = 0.2617e^0.0486x
0
20
40
60
80
100
Temperature C

Figure 2

Exp. #	Charge		Nucl'n Temp.	Isolation Temp & Hold Time	Product Isolation: Ratio of % (-)-CPTA		Calculated %Yield of (-)-CPTA	Comments
	g iPA/ gCPTA	mole base/ mole CPTA			Crystal	M.L.		
1	4.11	0.57	61°	17° + 6hr	79.9	27.0	69.5	(+)-Salt nucleation at 22°
2	4.11	0.55	59°	22° + 8hr	77.9	28.3	68.2	(+)-Salt nucleation after 1 hr at 22°
3	4.11	0.90	59°	40°	99.2	27.7	61.9	initially added 0.15 eq. triethylamine
4	5.50	0.75	61°	22° + 10hr	66.4	30.7	71.8	(+)-Salt nucleation at 40°
				to 28°	68.2	28.8	73.4	
				to 35°	71.4	29.1	70.6	
				to 43°	77.0	29.9	65.7	
				to 51°	95.0	30.3	57.9	
				to 55°	99.4	33.0	50.9	
5	4.11	0.52	61°	13° + 8hr	99.7	20.9	73.6	(+)-Salt nucleation 3 hr after sample
				+ 30hr (13°)	83.3	24.9	71.6	
6	3.14	0.52	59°	1°	98.7	23.5	69.6	
				+20hr(1°)	98.2	19.4	76.3	
				to 17° + 9hr	81.2	25.3	71.8	
7	5.50	0.90	64°	3° + 1hr	66.4	25.5	79.6	initially added 0.04 eq. KOH
				to 22° + 10hr	~56	25.5	90.0	
8	3.53	0.55	59°	22° + 5hr	78.6	26.0	71.7	(+)-Salt nucleation at 30°
9	3.93	0.45	59°	22° + 4hr	99.6	24.3	68.0	
				+ 12hr (22°)	99.5	22.9	70.4	
		0.52 (added base)		(22°) + 3hr	89.4	24.6	70.1	(+)-Salt nucleating, not at equilibrium
		0.49 (added CPTA)		(22°) + 22hr	84.3	25.9	69.6	
10	3.53	0.52	59°	22° + 10hr	73.9	25.5	74.8	(+)-Salt nucleation at 25°
11	3.93	0.45	54°	22° + 14hr	99.1	22.6	71.0	
		0.48 (added base)		22° + 24hr	89.2	24.7	70.0	
12	3.93	0.43	52°	21°	99.5	27.5	62.2	
				+ 16hr (21 °)	99.4	23.9	68.7	seeded with (+)-Salt after sample
				+8hr(22°)	99.3	23.7	69.1	
		0.45 (added base)		22° + 14hr	98.9	22.5	71.2	seeded with (+)-Salt after sample
				+6hr(22°)	98.7	22.3	71.61	
		0.47 (added base)		22° + 14hr	96.8	21.9	72.6	seeded with (+)-Salt after sample
				+ 23hr (22°)	92.3	23.4	71.3	
13	3.14	0.38	59°	17° + 8hr	99.4	27.2	62.8	
				to -10° + 19hr	99.8	24.3	67.9	seeded with (+)-Salt after reaching 10°

Figure 3

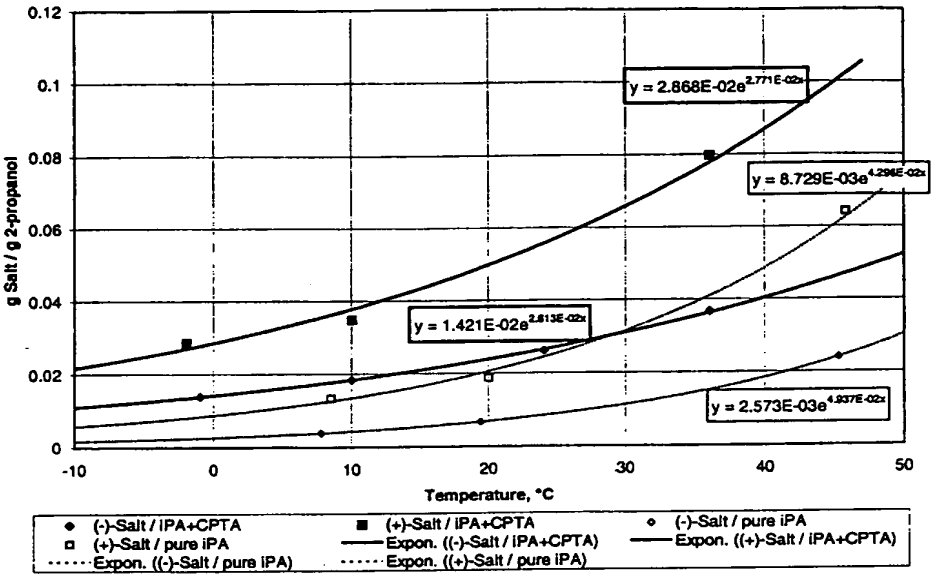
0.12
0.1
0.08
0.06
0.04
0.02
0
g Salt / g 2-propanol
-10
0
10
20
30
40
50
Temperature, °C
y = 2.868E-02e^2.771E-02x
y = 8.729E-03e^4.296E-02x
y = 1.421E-02e^2.813E-02x
y = 2.573E-03e^4.937E-02x
(-)-Salt / IPA+CPTA
(+)-Salt / IPA+CPTA
(-)-Salt / pure iPA
(+)-Salt / pure iPA
Expon. ((-)-Salt / IPA+CPTA)
Expon. ((+)-Salt / iPA+CPTA)
Expon. ((-)-Salt / pure iPA)
Expon. ((+)-Salt / pure iPA)

Figure 4

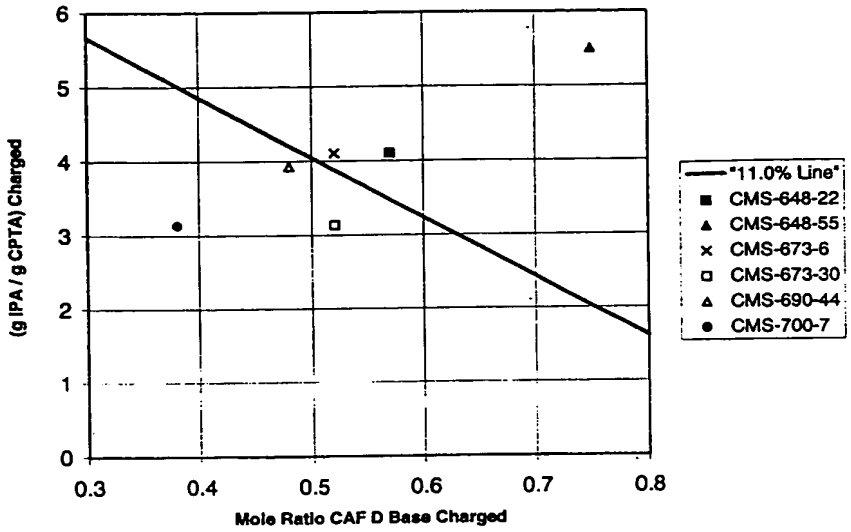
6
5
4
3
2
1
0
0.3
0.4
0.5
0.6
0.7
0.8
(g IPA / g CPTA) Charged
Mole Ratio CAF D Base Charged
"11.0% Line"
CMS-648-22
CMS-648-55
CMS-673-6
CMS-673-30
CMS-690-44
CMS-700-7

Figure 5

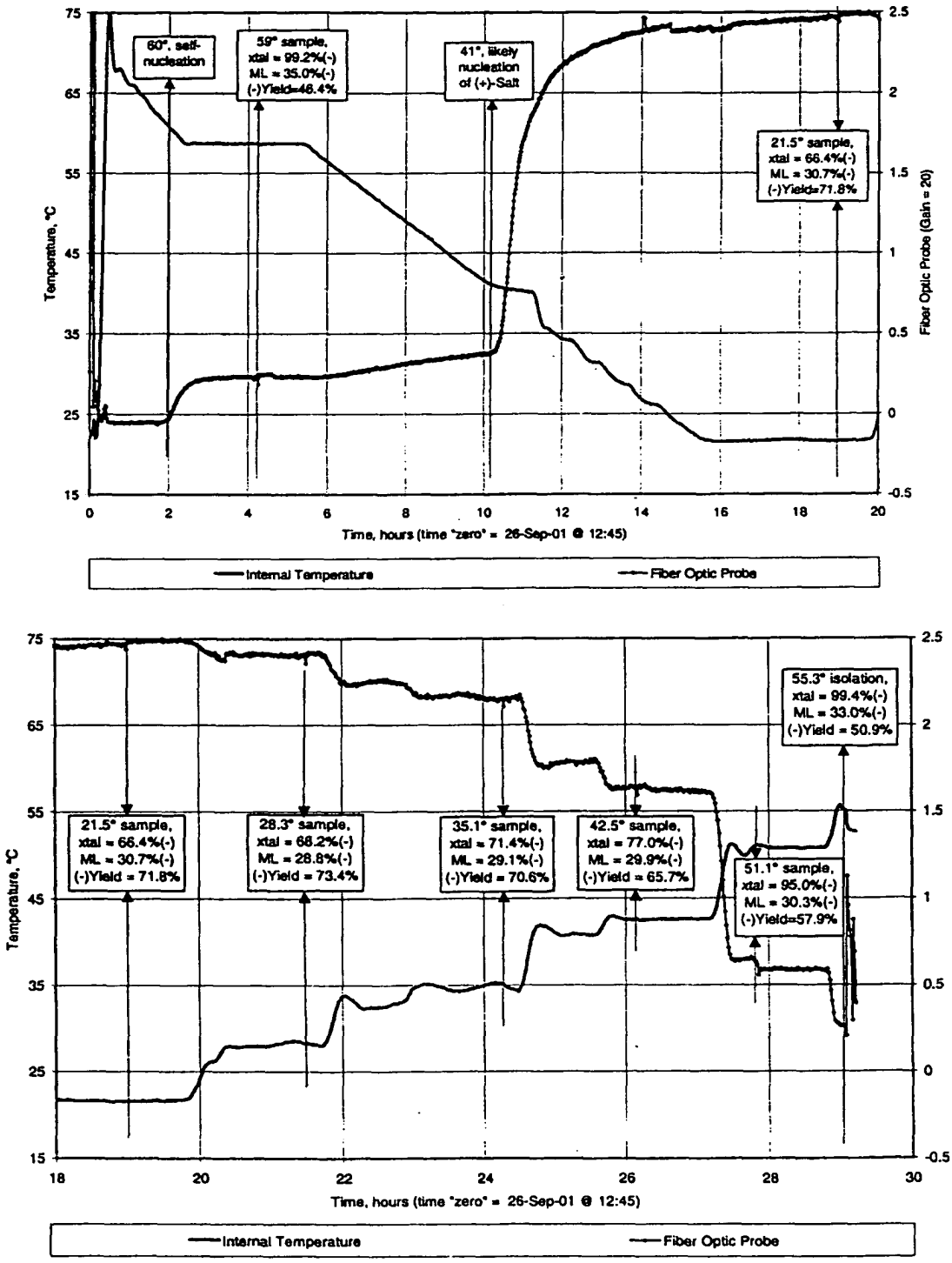
60°, self-nucleation
59° sample, xtal = 99.2%(-) ML = 35.0%(-) (-)Yield=46.4%
41°, likely nucleation of (+)-Salt
21.5° sample, xtal = 66.4%(-) ML = 30.7%(-) (-)Yield=71.8%
Temperature, °C
Fiber Optic Probe (Gain = 20)
Time, hours (time "zero" = 26-Sep-01 @ 12:45)
Internal Temperature
Fiber Optic Probe
21.5° sample, xtal = 66.4%(-) ML = 30.7%(-) (-)Yield = 71.8%
28.3° sample, xtal = 68.2%(-) ML = 28.8%(-) (-)Yield = 73.4%
35.1° sample, xtal = 71.4%(-) ML = 29.1%(-) (-)Yield = 70.6%
42.5° sample, xtal = 77.0%(-) ML = 29.9%(-) (-)Yield = 65.7%
55.3° isolation, xtal = 99.4%(-) ML = 33.0%(-) (-)Yield = 50.9%
51.1° sample, xtal = 95.0%(-) ML = 30.3%(-) (-)Yield=57.9%
Temperature, °C
Fiber Optic Probe (Gain = 20)
Time, hours (time "zero" = 26-Sep-01 @ 12:45)
Internal Temperature
Fiber Optic Probe

Figure 6

Temperature	Measured Component	Experimental Result	Calculation By Model
21.5 °C	Ratio % (-)-CPTA in crystal	66.4%	63.9%
	Ratio % (-)-CPTA in mother liquor	30.7%	28.5%
	% (-)-CPTA yield	71.8%	72.8%
28.3 °C	Ratio % (-)-CPTA in crystal	68.2%	68.2%
	Ratio % (-)-CPTA in mother liquor	28.8%	28.7%
	% (-)-CPTA yield	73.4%	73.6%
35.1 °C	Ratio % (-)-CPTA in crystal	71.4%	71.4%
	Ratio % (-)-CPTA in mother liquor	29.1%	28.9%
	% (-)-CPTA yield	70.6%	70.8%
42.5 °C	Ratio % (-)-CPTA in crystal	77.0%	76.7%
	Ratio % (-)-CPTA in mother liquor	29.9%	29.1%
	% (-)-CPTA yield	65.7%	67.4%
51.1 °C	Ratio % (-)-CPTA in crystal	95.0%	87.3%
	Ratio % (-)-CPTA in mother liquor	30.3%	29.2%
	% (-)-CPTA yield	57.9%	62.4%
55.3 °C	Ratio % (-)-CPTA in crystal	99.4%	96.1%
	Ratio % (-)-CPTA in mother liquor	33.0%	29.3%
	% (-)-CPTA yield	50.9%	59.6%

Figure 7

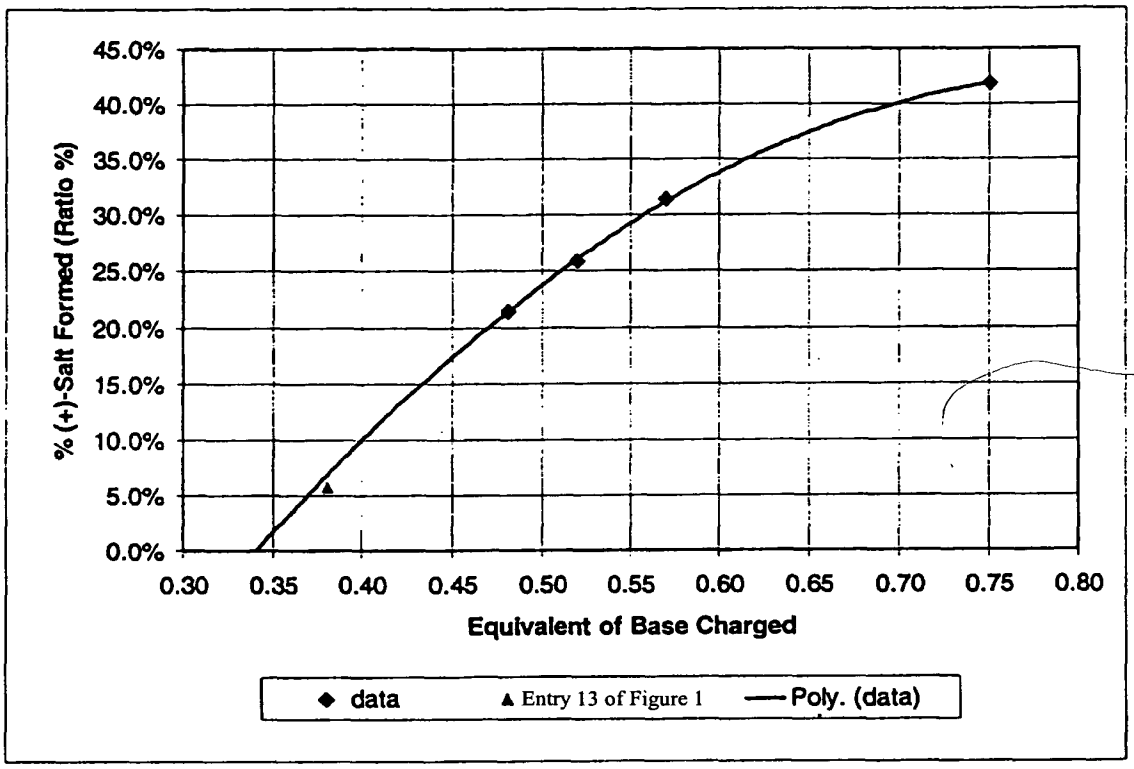
45.0%
40.0%
35.0%
30.0%
25.0%
20.0%
15.0%
10.0%
5.0%
0.0%
% (+)-Salt Formed (Ratio %)
0.30
0.35
0.40
0.45
0.50
0.55
0.60
0.65
0.70
0.75
0.80
Equivalent of Base Charged
◆ data
▲ Entry 13 of Figure 1
Poly. (data)

Figure 8

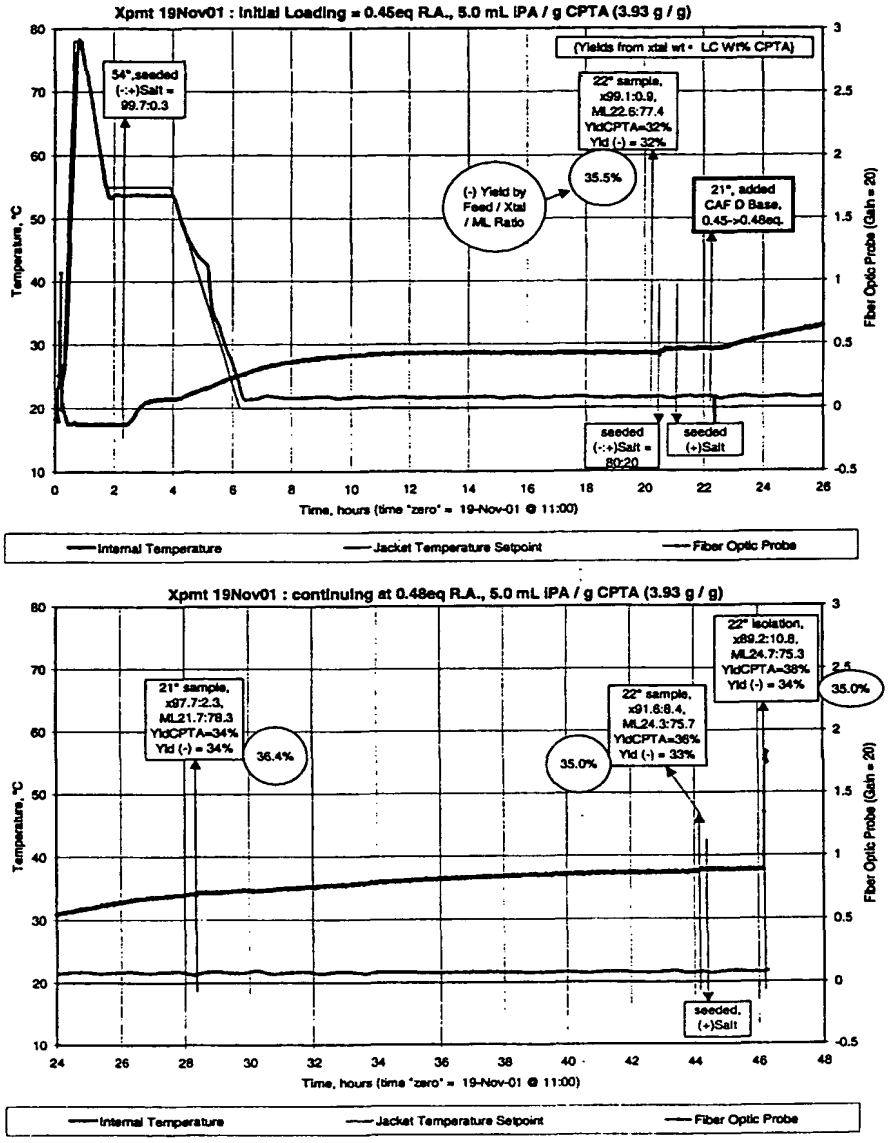
Xpmt 19Nov01 : Initial Loading = 0.45eq R.A., 5.0 mL IPA / g CPTA (3.93 g / g)
(Yields from xtal wt • LC Wt% CPTA)
54°,seeded (-:+)Salt = 99.7:0.3
22° sample, x99.1:0.9, ML22.6:77.4 YldCPTA=32% Yld (-) = 32%
35.5%
(-) Yield by Feed / Xtal / ML Ratio
21°, added CAF D Base, 0.45->0.48eq.
seeded (-:+)Salt = 80:20
seeded (+)Salt
Temperature, °C
Fiber Optic Probe (Gain = 20)
Time, hours (time "zero" = 19-Nov-01 @ 11:00)
Internal Temperature
Jacket Temperature Setpoint
Fiber Optic Probe
Xpmt 19Nov01 : continuing at 0.48eq R.A., 5.0 mL IPA / g CPTA (3.93 g / g)
21° sample, x97.7:2.3, ML21.7:78.3 YldCPTA=34% Yld (-) = 34%
36.4%
22° sample, x91.6:8.4, ML24.3:75.7 YldCPTA=36% Yld (-) = 33%
35.0%
22° isolation, x89.2:10.8, ML24.7:75.3 YldCPTA=38% Yld (-) = 34%
35.0%
seeded, (+)Salt
Temperature, °C
Fiber Optic Probe (Gain = 20)
Time, hours (time "zero" = 19-Nov-01 @ 11:00)
Internal Temperature
Jacket Temperature Setpoint
Fiber Optic Probe

Figure 9

	Normalized Wt% (as CPTA) in Mother Liquor	
Component	By Work-up	By Model
(-)-Salt	28%	20%
(+)-Salt	41%	44%
(-)-CPTA	7%	9%
(+)-CPTA	24%	27%

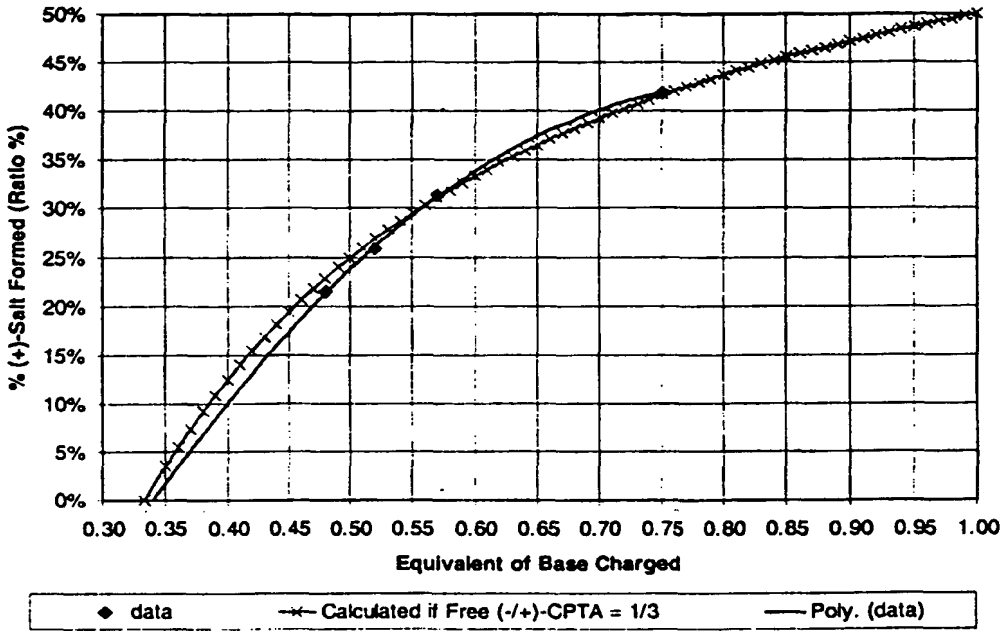

Figure 10A

(-)-CPTA • CAF D Base Salt : m.p. 180½-181½													
					Calculated Values								
	Temp.	grams	grams	grams	grams	grams	grams	grams	grams	Wt%	wt%solute	g solute/	
Solvent	°C	tare	w/soln	evap'd	soln	volat. solv	solids	CPTA	solute	solute	in evapSolv	g evap solv	
iPA w/CPTA	36	17.2900	18.0100	17.3895	0.7200	0.6205	0.0995	0.0767	0.0228	3.17%	3.55%	0.036755	
iPA w/CPTA	24	16.7808	17.5728	16.8840	0.7920	0.6888	0.1032	0.0851	0.0181	2.28%	2.56%	0.026226	
iPA w/CPTA	10	17.2556	18.1769	17.3702	0.9213	0.8067	0.1146	0.0997	0.0149	1.62%	1.81%	0.01846	
iPA w/CPTA	-1	17.1063	17.9898	17.2131	0.8835	0.7767	0.1068	0.0960	0.0108	1.22%	1.37%	0.013905	
EtOH w/CPTA	36	17.1900	17.9419	17.3577	0.7519	0.5842	0.1677	0.0912	0.0765	10.18%	11.58%	0.130959	
EtOH w/CPTA	24	17.2524	17.9330	17.3813	0.6806	0.5517	0.1289	0.0861	0.0428	6.29%	7.20%	0.077541	
EtOH w/CPTA	10	17.2977	18.1608	17.4587	0.8631	0.7021	0.1610	0.1096	0.0514	5.96%	6.82%	0.073212	
EtOH w/CPTA	-1	17.1536	18.2098	17.3383	1.0562	0.8715	0.1847	0.1360	0.0487	4.61%	5.29%	0.055833	

(+)-CPTA • CAF D Base Salt													
					Calculated Values								
	Temp.	grams	grams	grams	grams	grams	grams	grams	grams	Wt%	wt%solute	g solute/	
Solvent	°C	tare	w/soln	evap'd	soln	solvent	solids	CPTA	solute	solute	in evapSolv	g evap solv	
iPA w/CPTA	-2	17.2325	17.8545	17.3147	0.6220	0.5398	0.0822	0.0667	0.0155	2.49%	2.79%	0.028679	
iPA w/CPTA	10	17.1810	17.7942	17.2649	0.6132	0.5293	0.0839	0.0654	0.0185	3.01%	3.37%	0.034911	
iPA w/CPTA	22	17.2838	18.0462	17.4053	0.7624	0.6409	0.1215	0.0792	0.0423	5.55%	6.19%	0.065977	
iPA w/CPTA	36	17.1474	17.8976	17.2742	0.7502	0.6234	0.1268	0.0771	0.0497	6.63%	7.39%	0.079801	
	10	17.2816	17.4692	17.3074	0.1876	0.1618	0.0258	0.0200	0.0058	3.09%	3.46%	0.035856	
EtOH w/CPTA	-2	17.3289	18.5380	17.6105	1.2091	0.9275	0.2816	0.1448	0.1368	11.32%	12.85%	0.147512	
EtOH w/CPTA	10	17.2118	17.9940	17.4089	0.7822	0.5851	0.1971	0.0913	0.1058	13.52%	15.31%	0.180765	
EtOH w/CPTA	22	17.2095	18.0054	17.4362	0.7959	0.5692	0.2267	0.0889	0.1378	17.32%	19.50%	0.242178	
EtOH w/CPTA	36	17.2133	17.9657	17.4487	0.7524	0.5170	0.2354	0.0807	0.1547	20.56%	23.03%	0.299219	

Experimental Data for Figure 6

Eq. Base	Predicted *k*	Regression *k* used	Regression % (+)-Salt	Free CPTA, Ratio % (+)
0.75	<1	0.68	41.9	25.8
0.57	<1	0.85	31.4	25.3
0.52	<1	0.70	25.7	23.7
0.52	>1	0.60	26.1	24.1
0.48	>1	0.50	21.5	23.7

Figure 10B

Eq Base				k Factor			Salt in IPA+CPTA		(+)	(-)			
0.75	(-)	0.4354	58.1%	orig	0.02869	ln(S) = a + bT		e^a =	0.019509	0.009663			
				new	0.019509	S = e^a*e^bT		a =	-3.93687	-4.63947	0.01421	orig	
								b =	0.02771	0.02613	0.009663	new	
Basis: Salt in Solvent													
							Calc	Calc	Calc °C	Calc		ML	actual
g iPA	Wt_Fract	Feed,	Feed,	G(+) /	G(-) /	Isolation	soluble	insoluble	Temp of	soluble	insoluble	ratio	insoluble
/g Solute	solute	% (+)	% (-)	G iPA	G iPA	T, °C	(+)	(+)	(+) Sat'n	(-)	(-)	(+)	(+)
4.465696	0.182959	0.419467	0.580533	0.093931	0.129998	28.30	0.042738	0.051193	56.72	0.020242	0.109758	67.86%	0.05119
						(based on							
						Avail. (-))			Calc °C	salt			
						Crystal	%(+)	%(-)	Temp of	grav			
						Yield	in Xtal	in Xtal	(-) Sat'n	yield			
						123.8%	31.81%	68.19%	99.47	71.9%			

Mass Balance for 100g CPTA Fed			Salt	CPTA		grams	Ratio%				
	salt	saltML	sum	in ML		overallML	overallML				
(-)ratio	68.19299	32.14063									
(+)ratio	31.80701	67.85937									
weight	0.539064	0.210936						grav yield from CPTA =		53.9%	
					Ratio			(-)yield from CPTA =		36.8%	
100g total CPTA feed					%						
g (-)	36.76038	6.779616	43.54	6.46	25.8%	13.23962	28.7%				
g (+)	17.14601	14.31399	31.46	18.54	74.2%	32.85399	71.3%				
total	53.9064	21.0936	75	25		46.0936					

Figure 11

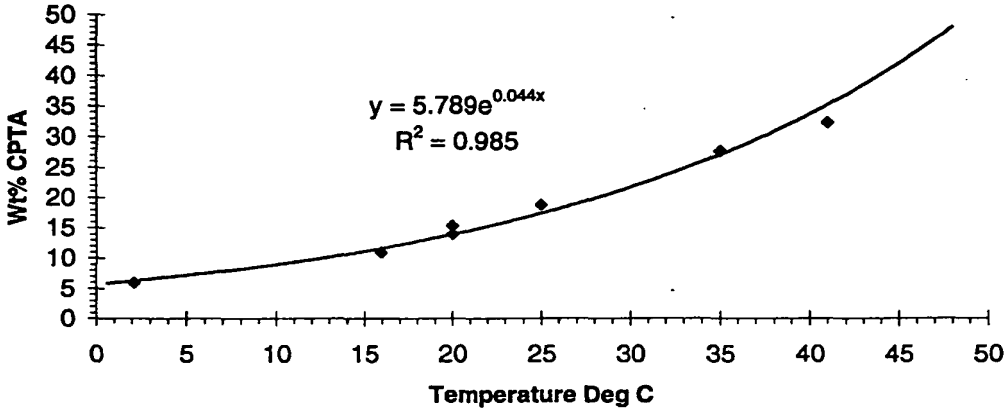
y = 5.789e^0.044x
R^2 = 0.985
Wt% CPTA
Temperature Deg C
0
5
10
15
20
25
30
35
40
45
50

Figure 12

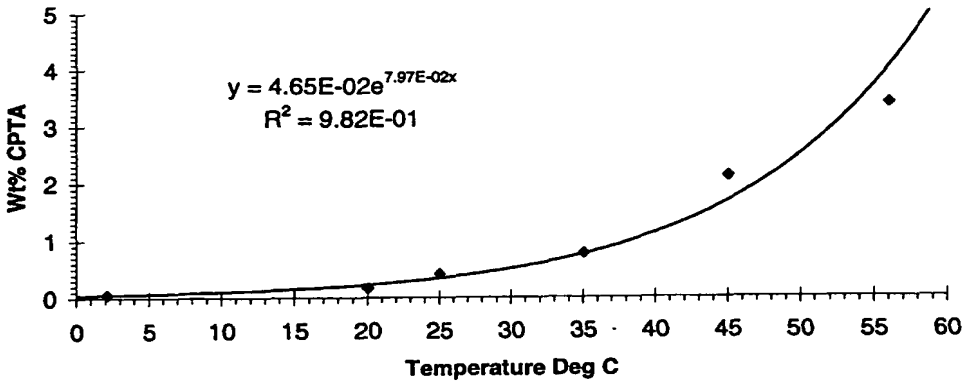
y = 4.65E-02e^7.97E-02x
R² = 9.82E-01
Wt% CPTA
Temperature Deg C
0
1
2
3
4
5
0
5
10
15
20
25
30
35
40
45
50
55
60

Figure 13

Exp. #	MolRatio Base	g IPA/ g CPTA	Cool at °C/min	Final T °C	Solid % (-)	Solid % (+)	M.L. % (-)	M.L. % (+)	%Yield Calc	%Yield Overall	%Yield Actual
1	0.53	4.00	0.25	4	90.72	9.28	20.61	79.39	41.9		
Recrystallization		4.00	0.25-1.0	2	**99.38**	**0.62**	42.60	57.40	84.7	35.5	34.5
2	0.50	6.17	0.05	-3	**98.05**	**1.95**	24.05	75.95	35.1	35.1	33.6
3	0.53	4.00	0.25	0	73.14	26.86	28.88	71.12	47.7		
Recrystallization		4.00	1.0	11	**98.20**	**1.80**	22.62	77.38	66.8	31.9	33.0
4	0.54	4.00	0.25	-4	79.72	20.28	26.62	73.38	44.0		
Recrystallization		3.63	0.08	4	**99.07**	**0.93**	23.22	76.78	74.5	32.8	32.8
5	0.53	4.00	0.5	-11	93.70	6.30	26.00	74.00	35.4		
Recrystallization		3.93	0.5	-3	**99.68**	**0.33**	46.42	53.58	88.8	31.5	31.6
6	0.53	3.98	0.25	-3	90.88	9.12	26.95	73.05	36.1		
Recrystallization		4.98	0.1	4	**99.42**	**0.58**	23.85	76.15	88.7	32.0	31.5
7	0.54	4.08	0.3	-3	96.00	4.00	nd	nd	-		
Recrystallization		4.24	0.4	4	**99.86**	**0.14**	57.41	42.59	90.9	-	31.2
8	0.53	4.00	0.25	-8	73.54	26.46	28.09	71.91	48.2		
Recrystallization		3.96	0.3	11	**98.57**	**1.43**	21.84	78.16	67.4	32.5	31.1
9	0.50	3.88	0.08	-7	76.83	23.17	28.96	71.04	43.9		
Recrystallization		4.62	0.5	5	**98.48**	**1.52**	24.91	75.09	70.6	31.0	30.7
10	0.50	3.90	0.05	0	96.15	3.85	26.07	73.93	34.1		
Recrystallization		4.80	0.3	3	**99.86**	**0.14**	70.32	29.68	87.4	29.9	30.6
11	0.55	6.16	0.2	5	73.92	26.08	nd	nd	-		
Recrystallization		4.38	0.08	12	**99.31**	**0.69**	41.08	58.92	56.4	-	29.1
12	0.56	4.99	0.1	2	78.92	21.08	28.04	71.96	43.2		
Recrystallization		5.00	0.25	4	84.47	15.53	29.29	70.71	89.9	(38.8)	(38.3)
Recrystallization		5.00	0.25	12	**99.44**	**0.56**	30.30	69.70	78.4	30.4	28.2

nd – Not Determined

Figure 14

Exp. # (Fig. 1)	Initial T °C	Rate °C/min	Final T °C	Hrs at < 10 °C	Holding Period Profile	Solid % (-)	Solid % (+)	M.L. % (-)	M.L. % (+)	% Yield (-)-CPTA
1	60	0.25	4	14	13h at 4C	90.72	9.28	20.61	79.39	38.0
8	60	0.25	-5	20	11 h to 10C; 3h to -8C, 5h at -8C	73.54	26.46	28.09	71.91	35.5
4	55	0.25	-4	3	1h at -4C	79.72	20.28	26.62	73.38	35.1
3	60	0.25	-2	16	11h to 10C; 1h to -2C, 4h at -2C	73.14	26.86	28.88	71.12	34.9
2	55	0.05	-3	5	1h at -3C	98.05	1.95	24.05	75.95	34.4
12	55	0.10	1	13	9h to 10C; 1h to 1C; 4h at 1C	78.92	21.08	28.04	71.97	34.1
9	65	0.075	0	8	3h at 0C; 1h to -7C; 2h at -7C	76.83	23.17	28.96	71.04	33.8
5	60	0.5	-11	2.5	1.5h at -11C	93.70	6.30	26.00	74.00	33.2
10	55	0.05	0	4	1h at 0C	96.15	3.85	26.07	73.93	32.8
6	55	0.25	-3	2	1h at -3C	90.88	9.12	26.95	73.05	32.8

Figure 15

	%ee		HPLC Area% Crude		HPLC Area% Isolated			mol % in ML	
	CPTA	(-)-halofenate	CPTA	Halofenate	CPTA	Halofenate	Yield	CPTA	Halofenate
1	97.1	99.9	6.1	85.2	0.72	98.93	55%	5.8%	38%
2	99.3	>99.8	5.5	89.6	0.60	99.40	52%	5.9%	41%
Second Crop		99.6	6.1	45.0	3.89	89.93	21%	4.3%	13%
3	99.2	99.7	7.1	85.3	0.40	99.29	55%	7.5%	34%
4	98.6	99.8	3.9	91.8	0.10	99.90	47%	3.1%	40%
Second Crop		98.8	6.1	82.5	3.22	89.65	33%	nd	nd
5	99.7	99.7	8.0	83.2	0.64	99.18	59%	nd	nd

nd – Not Determined

Figure 16

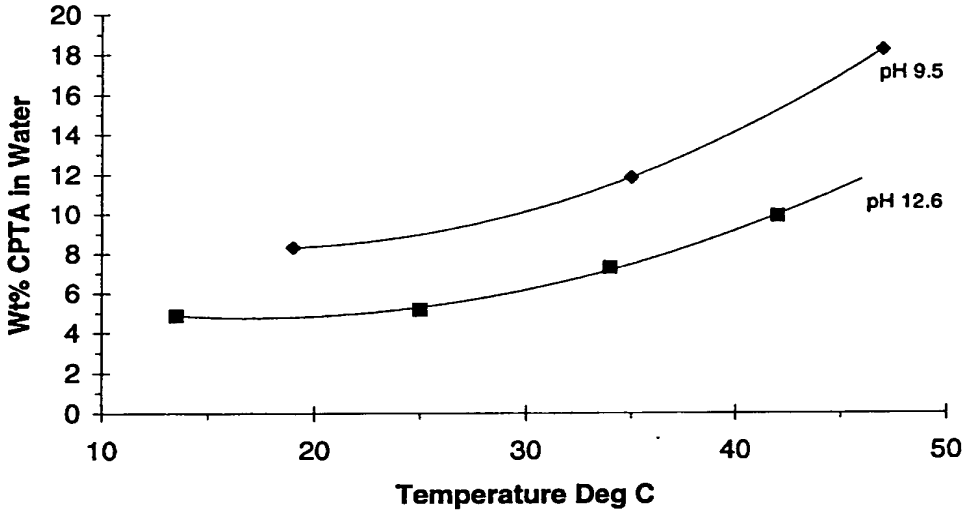
Wt% CPTA in Water
20
18
16
14
12
10
8
6
4
2
0
10
20
30
40
50
Temperature Deg C
pH 9.5
pH 12.6

Figure 17

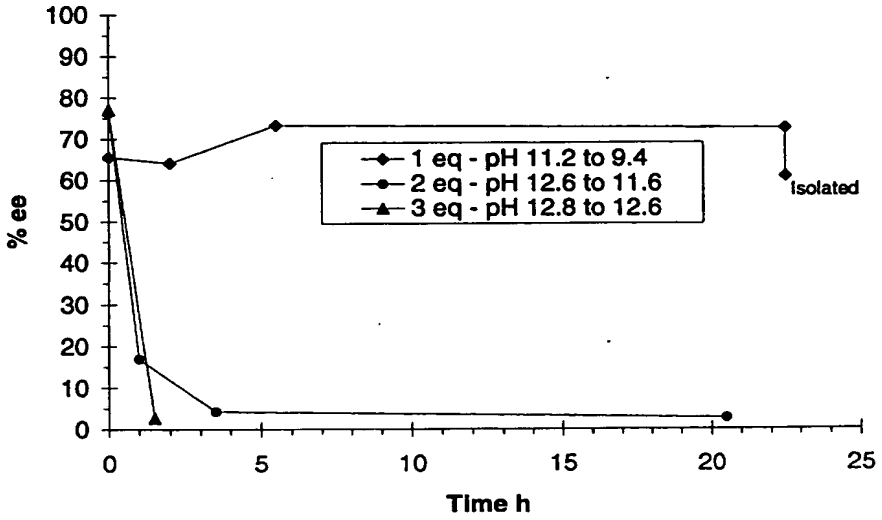
100
90
80
70
60
50
40
30
20
10
0
% ee
0
5
10
15
20
25
Time h
1 eq - pH 11.2 to 9.4
2 eq - pH 12.6 to 11.6
3 eq - pH 12.8 to 12.6
Isolated

Figure 18

Recovered From:	Wt% Aqueous Sln	pH	mp °C	Recovery	(+)/(-) Ratio
Diastereomeric Salt	20.4	12.4	157.2-158.0	97%	0.1/99.9
"	20.1	12.1	160.4-161.0	98%	
"	19.6	nd	164.0-164.6	92%	
"	11.9	13.2	161.8-162.6	94%	
"	4.1	12	164.0-164.6	88%	0.1/99.9
Resolution ML	13.9	13	159.2-159.6	62%	
"	11.0	12.3	162.4-163.0	87%	
Combined ML & Salt	19.9	13	162.6-163.4	85%	
	TCI Americas Lot# FHG01		165.6-166.4		0.1/99.9

Figure 19

Solvent	Temp °C	Sample weight g	Sample Volume mL	Wt% CPTA in Solution
1,2-Dichloroethane	41	0.1558	25.00	32.3
	35	0.1360	25.00	27.6
	25	0.1455	10.00	18.8
	20	0.0489	25.00	15.3
	20	0.0505	10.00	14.0
	16	0.3230	25.00	11.0
	2.1	0.1300	10.00	6.05
Heptane	56	0.4641	25.00	3.39
	45	0.3331	25.00	2.11
	35	0.3823	25.00	0.767
	25	0.6750	25.00	0.413
	20	0.1994	10.00	0.17
	2.1	0.6038	25.00	0.057

Figure 20

pH	Temp °C	Sample weight g	Sample Volume mL	Wt% CPTA in Solution
9.4	35	0.3036	25.00	11.86
9.7	47	0.1111	25.00	18.28
9.5	19	0.2290	25.00	8.33
12.7	13.5	0.2012	25.00	4.89
12.6	25	0.3538	25.00	5.18
12.5	34	0.2320	25.00	7.30
12.5	42	0.3055	25.00	9.91

Figure 21

Wt Loaded g				HPLC Area%	% CPTA	
(+)-Halofenate	50% NaOH	Reflux Time	pH	(+) / (-)	Assay	Isolated
8.65	1.67 (1 eq)	0 h	11.2	71.9/15.1		
		2		78.3/17.2		
		5.5		80.6/12.4		
		22.5	9.4	84.1/13.4		
		Oil		80.3/19.6	92%	81%
6.94	2.68 (2 eq)	0	12.6	83.4/11.3		
		1		56.8/40.4		
		3.5		49.0/45.0		
		20.5	11.6	47.5/45.0		
		Oil		48.7/51.0	103%	94%
7.28	4.21 (3 eq)	0	12.8	80.4/10.5		
		1.5	12.6	49.6/47.0		
		Oil		47.3/52.5	102%	88%